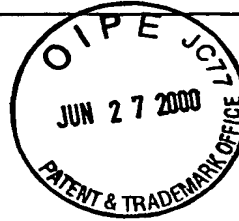


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## SEQUENCE LISTING



<110> WALLACH, David  
GOLTSEV, Yura  
KOVALENKO, Andrei  
VARFOLOMEEV, Eugene  
BRODIANSKI, Vadim

<120> CASH (CASPASE HOMOLOGUE) WITH DEATH EFFECTOR DOMAIN,  
MODULATORS OF THE FUNCTION OF FAS RECEPTORS

<130> WALLACH=23

<140> 09/380,546

<141> 1999-11-29

<150> PCT/IL98/00098

<151> 1998-02-26

<150> IL 120367

<151> 1997-03-03

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<170> PatentIn Ver. 2.0

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Val Pro Pro Asn Val Arg Asp Leu Leu Asp Ile Leu Arg Glu Arg Gly
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Lys Leu Ser Val Gly Asp Leu Ala Glu Leu Leu Tyr Arg Val Arg Arg
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Phe Asp Leu Leu Lys Arg Ile Leu Lys Met Asp Arg Lys Ala Val Glu
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Thr His Leu Leu Asn Pro His Leu Val Ser Asp Tyr Arg Val Leu Met
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Phe Leu Met Lys Asp Tyr Met Gly Arg Gly Lys Ile Ser Lys Glu Lys
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 Asp Cys Ile Gly Asn Glu Thr Glu Leu Leu Arg Asp Thr Phe Thr Ser  
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 Ser Gln Ile Leu Gly Gln Phe Ala Cys Met Pro Glu His Arg Asp Tyr  
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 Tyr Gly Val Asp Gln Thr His Ser Gly Leu Pro Leu His His Ile Arg  
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 Arg Met Phe Met Gly Asp Ser Cys Pro Tyr Leu Ala Gly Lys Pro Lys  
 340 345 350  
 Met Phe Phe Ile Gln Asn Tyr Val Val Ser Glu Gly Gln Leu Glu Asn  
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 Ser Ser Leu Leu Glu Val Asp Gly Pro Ala Met Lys Asn Val Glu Phe  
 370 375 380  
 Lys Ala Gln Lys Arg Gly Leu Cys Thr Val His Arg Glu Ala Asp Phe  
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 Ser Ser Pro Ser Leu Tyr Leu Gln Cys Leu Ser Gln Lys Leu Arg Gln  
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 Glu Arg Lys Arg Pro Leu Leu Asp Leu His Ile Glu Leu Asn Gly Tyr  
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 Val Pro Pro Asn Val Arg Asp Leu Leu Asp Ile Leu Arg Glu Arg Gly  
 35 40 45  
 Lys Leu Ser Val Gly Asp Leu Ala Glu Leu Leu Tyr Arg Val Arg Arg  
 50 55 60  
 Phe Asp Leu Leu Lys Arg Ile Leu Lys Met Asp Arg Lys Ala Val Glu  
 65 70 75 80  
 Thr His Leu Leu Arg Asn Pro His Leu Val Ser Asp Tyr Arg Val Leu  
 85 90 95  
 Met Ala Glu Ile Gly Glu Asp Leu Asp Lys Ser Asp Val Ser Ser Leu  
 100 105 110

Ile Phe Leu Met Lys Asp Tyr Met Gly Arg Gly Lys Ile Ser Lys Glu  
 115 120 125  
 Lys Ser Phe Leu Asp Leu Val Val Glu Leu Glu Lys Leu Asn Leu Val  
 130 135 140  
 Ala Pro Asp Gln Leu Asp Leu Leu Glu Lys Cys Leu Lys Asn Ile His  
 145 150 155 160  
 Arg Ile Asp Leu Lys Thr Lys Ile Gln Lys Tyr Lys Gln Ser Val Gln  
 165 170 175  
 Gly Ala Gly Thr Ser Tyr Arg Asn Val Leu Gln Ala Ala Ile Gln Lys  
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 Leu Ser Glu Arg Gly Gln Leu Ser Phe Ala Thr Leu Ala Glu Leu Leu  
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 Tyr Arg Val Arg Arg Phe Asp Leu Leu Lys Arg Ile Leu Lys Thr Asp  
 65 70 75 80  
 Lys Ala Thr Val Glu Asp His Leu Arg Arg Asn Pro His Leu Val Ser  
 85 90 95  
 Asp Tyr Arg Val Leu Leu Met Glu Ile Gly Glu Ser Leu Asp Gln Asn  
 100 105 110  
 Asp Val Ser Ser Leu Val Phe Leu Thr Arg Ile Thr Arg Asp Tyr Thr  
 115 120 125  
 Gly Arg Gly Lys Ile Ala Lys Asp Lys Ser Phe Leu Asp Leu Val Ile  
 130 135 140  
 Glu Leu Glu Lys Leu Asn Leu Ile Ala Ser Asp Gln Leu Asn Leu Leu  
 145 150 155 160

Glu Lys Cys Leu Lys Asn Ile His Arg Ile Asp Leu Asn Thr Lys Ile  
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 Gln Lys Tyr Thr Gln Ser Ser Gln Gly Ala Arg Ser Asn Met Asn Thr  
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 225 230 235 240  
 Pro Pro His Ile Arg Glu Glu Thr Tyr Arg Met Gln Ser Lys Pro Leu  
 245 250 255  
 Gly Ile Cys Leu Ile Ile Asp Cys Ile Gly Asn Asp Thr Lys Tyr Leu  
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 Gln Glu Thr Phe Thr Ser Leu Gly Tyr His Ile Gln Leu Phe Leu Phe  
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 Ala Gln His Gln Asp Tyr Asp Ser Phe Ala Cys Val Leu Val Ser Leu  
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 Ser Leu Asp His Val Lys Asn Met Phe Thr Gly Asp Thr Cys Pro Ser  
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 Pro Glu Ala Asp Ile Phe Trp Ser Leu Cys Thr Ala Asp Val Ser His  
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 420 425 430  
 Gln Gln Leu Lys Gln Gly Arg Arg Arg Pro Leu Val Asp Leu His Val  
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 Glu Leu Met Asp Lys Val Tyr Ala Trp Asn Ser Gly Val Ser Ser Lys  
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Glu Lys Tyr Ser Leu Ser Leu Gln His Thr Leu Arg Lys Lys Leu Ile  
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<211> 221

<212> PRT

<213> Homo sapiens

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Val Pro Pro Asn Val Arg Asp Leu Leu Asp Ile Leu Arg Glu Arg Gly  
 35 40 45

Lys Leu Ser Val Gly Asp Leu Ala Glu Leu Leu Tyr Arg Val Arg Arg  
 50 55 60

Phe Asp Leu Leu Lys Arg Ile Leu Lys Met Asp Arg Lys Ala Val Glu  
 65 70 75 80

Thr His Leu Leu Arg Asn Pro His Leu Val Ser Asp Tyr Arg Val Leu  
 85 90 95

Met Ala Glu Ile Gly Glu Asp Leu Asp Lys Ser Asp Val Ser Ser Leu  
 100 105 110

Ile Phe Leu Met Lys Asp Tyr Met Gly Arg Gly Lys Ile Ser Lys Glu  
 115 120 125

Lys Ser Phe Leu Asp Leu Val Val Glu Leu Glu Lys Leu Asn Leu Val  
 130 135 140

Ala Pro Asp Gln Leu Asp Leu Leu Glu Lys Cys Leu Lys Asn Ile His  
 145 150 155 160

Arg Ile Asp Leu Lys Thr Lys Ile Gln Lys Tyr Lys Gln Ser Val Gln  
 165 170 175

Gly Ala Gly Thr Ser Tyr Arg Asn Val Leu Gln Ala Ala Ile Gln Lys  
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Ser Leu Lys Asp Pro Ser Asn Asn Phe Arg Met Ile Thr Pro Tyr Ala  
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His Cys Pro Asp Leu Lys Ile Leu Gly Asn Cys Ser Met  
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&lt;212&gt; PRT

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Val Pro Pro Asn Val Arg Asp Leu Leu Asp Ile Leu Arg Glu Arg Gly
      35             40             45

Lys Leu Ser Val Gly Asp Leu Ala Glu Leu Leu Tyr Arg Val Arg Arg
 50             55             60

Phe Asp Leu Leu Lys Arg Ile Leu Lys Met Asp Arg Lys Ala Val Glu
 65             70             75             80

Thr His Leu Leu Arg Asn Pro His Leu Val Ser Asp Tyr Arg Val Leu
      85             90             95

Met Ala Glu Ile Gly Glu Asp Leu Asp Lys Ser Asp Val Ser Ser Leu
      100             105             110

Ile Phe Leu Met Lys Asp Tyr Met Gly Arg Gly Lys Ile Ser Lys Glu
 115             120             125

Lys Ser Phe Leu Asp Leu Val Val Glu Leu Glu Lys Leu Asn Leu Val
 130             135             140

Ala Pro Asp Gln Leu Asp Leu Leu Glu Lys Cys Leu Lys Asn Ile His
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Arg Ile Asp Leu Lys Thr Lys Ile Gln Lys Tyr Lys Gln Ser Val Gln
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Gly Ala Gly Thr Ser Tyr Arg Asn Val Leu Gln Ala Ala Ile Gln Lys
      180             185             190

Ser Leu Lys Asp Pro Ser Asn Asn Phe Arg Leu His Asn Gly Arg Ser
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Lys Glu Gln Arg Leu Lys Glu Gln Leu Gly Ala Gln Gln Glu Pro Val
 210             215             220

Lys Lys Ser Ile Gln Glu Ser Glu Ala Phe Leu Pro Gln Ser Ile Pro
 225             230             235             240

Glu Glu Arg Tyr Lys Met Lys Ser Lys Pro Leu Gly Ile Cys Leu Ile
      245             250             255

Ile Asp Cys Ile Gly Asn Glu Thr Glu Leu Leu Arg Asp Thr Phe Thr
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Ser Leu Gly Tyr Glu Val Gln Lys Phe Leu His Leu Ser Met His Gly
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 Val Tyr Gly Val Asp Gln Thr His Ser Gly Leu Pro Leu His His Ile  
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 Arg Arg Met Phe Met Gly Asp Ser Cys Pro Tyr Leu Ala Gly Lys Pro  
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 Lys Met Phe Phe Ile Gln Asn Tyr Val Val Ser Glu Gly Gln Leu Glu  
 355 360 365  
 Asn Ser Ser Leu Leu Glu Val Asp Gly Pro Ala Met Lys Asn Val Glu  
 370 375 380  
 Phe Lys Ala Gln Lys Arg Gly Leu Cys Thr Val His Arg Glu Ala Asp  
 385 390 395 400  
 Phe Phe Trp Ser Leu Cys Thr Ala Asp Met Ser Leu Leu Glu Gln Ser  
 405 410 415  
 His Ser Ser Pro Ser Leu Tyr Leu Gln Cys Leu Ser Gln Lys Leu Arg  
 420 425 430  
 Gln Glu Arg Lys Arg Pro Leu Leu Asp Leu His Ile Glu Leu Asn Gly  
 435 440 445  
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<212> PRT

<213> Homo sapiens

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 Arg Lys Gln Glu Pro Ile Lys Asp Ala Leu Met Leu Phe Gln Arg Leu  
 35 40 45  
 Gln Glu Lys Arg Met Leu Glu Glu Ser Asn Leu Ser Phe Leu Lys Glu  
 50 55 60

Leu	Leu	Phe	Arg	Ile	Asn	Arg	Leu	Asp	Leu	Leu	Ile	Thr	Tyr	Leu	Asn	65	70	75	80
Thr	Arg	Lys	Glu	Glu	Met	Glu	Arg	Glu	Leu	Gln	Thr	Pro	Gly	Arg	Ala	85	90	95	
Gln	Ile	Ser	Ala	Tyr	Arg	Val	Met	Leu	Tyr	Gln	Ile	Ser	Glu	Glu	Val	100	105	110	
Ser	Arg	Ser	Glu	Leu	Arg	Ser	Phe	Lys	Phe	Leu	Leu	Gln	Glu	Glu	Ile	115	120	125	
Ser	Lys	Cys	Lys	Leu	Asp	Asp	Asp	Met	Asn	Leu	Leu	Asp	Ile	Phe	Ile	130	135	140	
Glu	Met	Glu	Lys	Arg	Val	Ile	Leu	Gly	Glu	Gly	Lys	Leu	Asp	Ile	Leu	145	150	155	160
Lys	Arg	Val	Cys	Ala	Gln	Ile	Asn	Lys	Ser	Leu	Leu	Lys	Ile	Ile	Asn	165	170	175	
Asp	Tyr	Glu	Glu	Phe	Ser	Lys	Glu	Arg	Ser	Ser	Ser	Leu	Glu	Gly	Ser	180	185	190	
Pro	Asp	Glu	Phe	Ser	Asn	Gly	Glu	Glu	Leu	Cys	Gly	Val	Met	Thr	Ile	195	200	205	
Ser	Asp	Ser	Pro	Arg	Glu	Gln	Asp	Ser	Glu	Ser	Gln	Thr	Leu	Asp	Lys	210	215	220	
Val	Tyr	Gln	Met	Lys	Ser	Lys	Pro	Arg	Gly	Tyr	Cys	Leu	Ile	Ile	Asn	225	230	235	240
Asn	His	Asn	Phe	Ala	Lys	Ala	Arg	Glu	Lys	Val	Pro	Lys	Leu	His	Ser	245	250	255	
Ile	Arg	Asp	Arg	Asn	Gly	Thr	His	Leu	Asp	Ala	Gly	Ala	Leu	Thr	Thr	260	265	270	
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Ser	Asn	Met	Asp	Cys	Phe	Ile	Cys	Cys	Ile	Leu	Ser	His	Gly	Asp	Lys	305	310	315	320
Gly	Ile	Ile	Tyr	Gly	Thr	Asp	Gly	Gln	Glu	Gly	Pro	Ile	Tyr	Glu	Leu	325	330	335	
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Lys	Val	Phe	Phe	Ile	Gln	Ala	Cys	Gln	Gly	Asp	Asn	Tyr	Gln	Lys	Gly	355	360	365	

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Lys Ile Asp Glu Asp Asn Leu Thr Cys Leu Glu Asp Leu Cys Lys Thr  
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 Val Val Pro Lys Leu Leu Arg Asn Ile Glu Lys Tyr Lys Arg Glu Lys  
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 Ala Ile Gln Ile Val Thr Pro Pro Val Asp Lys Glu Ala Glu Ser Tyr  
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 Gln Gly Glu Glu Glu Leu Val Ser Gln Thr Asp Val Lys Thr Phe Leu  
 210 215 220  
 Glu Ala Leu Pro Arg Ala Ala Val Tyr Arg Met Asn Arg Asn His Arg  
 225 230 235 240  
 Gly Leu Cys Val Ile Val Asn Asn His Ser Phe Thr Ser Leu Lys Asp  
 245 250 255  
 Arg Gln Gly Thr His Lys Asp Ala Glu Ile Leu Ser His Val Phe Gln  
 260 265 270  
 Trp Leu Gly Phe Thr Val His Ile His Asn Asn Val Thr Lys Val Glu  
 275 280 285  
 Met Glu Met Val Leu Gln Lys Gln Lys Cys Asn Pro Ala His Ala Asp  
 290 295 300  
 Gly Asp Cys Phe Val Phe Cys Ile Leu Thr His Gly Arg Phe Gly Ala  
 305 310 315 320  
 Val Tyr Ser Ser Asp Glu Ala Leu Ile Pro Ile Arg Glu Ile Met Ser  
 325 330 335  
 His Phe Thr Ala Leu Gln Cys Pro Arg Leu Ala Glu Lys Pro Lys Leu  
 340 345 350  
 Phe Phe Ile Gln Ala Cys Gln Gly Glu Glu Ile Gln Pro Ser Val Ser  
 355 360 365  
 Ile Glu Ala Asp Ala Leu Asn Pro Glu Gln Ala Pro Thr Ser Leu Gln  
 370 375 380  
 Asp Ser Ile Pro Ala Glu Ala Asp Phe Leu Leu Gly Leu Ala Thr Val  
 385 390 395 400  
 Pro Gly Tyr Val Ser Phe Arg His Val Glu Glu Gly Ser Trp Tyr Ile  
 405 410 415  
 Gln Ser Leu Cys Asn His Leu Lys Lys Leu Val Pro Arg His Glu Asp  
 420 425 430  
 Ile Leu Ser Ile Leu Thr Ala Val Asn Asp Asp Val Ser Arg Arg Val  
 435 440 445  
 Asp Lys Gln Gly Thr Lys Lys Gln Met Pro Gln Pro Ala Phe Thr Leu  
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Arg Lys Lys Leu Val Phe Pro Val Pro Leu Asp Ala Leu Ser Ile  
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Met Thr Ser Arg Ser Gly Thr Asp Val Asp Ala Ala Asn Leu Arg Glu  
 35 40 45

Thr Phe Arg Asn Leu Lys Tyr Glu Val Arg Asn Lys Asn Asp Leu Thr  
 50 55 60

Arg Glu Glu Ile Val Glu Leu Met Arg Asp Val Ser Lys Glu Asp His  
 65 70 75 80

Ser Lys Arg Ser Ser Phe Val Cys Val Leu Leu Ser His Gly Glu Glu  
 85 90 95

Gly Ile Ile Phe Gly Thr Asn Gly Pro Val Asp Leu Lys Lys Ile Thr  
 100 105 110

Asn Phe Phe Arg Gly Asp Arg Cys Arg Ser Leu Thr Gly Lys Pro Lys  
 115 120 125

Leu Phe Ile Ile Gln Ala Cys Arg Gly Thr Glu Leu Asp Cys Gly Ile  
 130 135 140

Glu Thr Asp Ser Gly Val Asp Asp Asp Met Ala Cys His Lys Ile Pro  
 145 150 155 160

Val Glu Ala Asp Phe Leu Tyr Ala Tyr Ser Thr Ala Pro Gly Tyr Tyr  
 165 170 175

Ser Trp Arg Asn Ser Lys Asp Gly Ser Trp Phe Ile Gln Ser Leu Cys  
 180 185 190

Ala Met Leu Lys Gln Tyr Ala Asp Lys Leu Glu Phe Met His Ile Leu  
 195 200 205

Thr Arg Val Asn Arg Lys Val Ala Thr Glu Phe Glu Ser Phe Ser Phe  
 210 215 220

Asp Ala Thr Phe His Ala Lys Lys Gln Ile Pro Cys Ile Val Ser Met  
 225 230 235 240

Leu Thr Lys Glu Leu Tyr Phe Tyr His  
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                   20                  25                  30  
 Ser Leu Glu Glu Ala Gln Arg Ile Trp Lys Gln Lys Ser Ala Glu Ile  
           35                          40                  45  
 Tyr Pro Ile Met Asp Lys Ser Ser Arg Thr Arg Leu Ala Leu Ile Ile  
       50                  55                  60  
 Cys Asn Glu Glu Phe Asp Ser Ile Pro Arg Arg Thr Gly Ala Glu Val  
   65                  70                  75                  80  
 Asp Ile Thr Gly Met Thr Met Leu Leu Gln Asn Leu Gly Tyr Ser Val  
                   85                  90                  95  
 Asp Val Lys Lys Asn Leu Thr Ala Ser Asp Met Thr Thr Glu Leu Glu  
                   100                  105                  110  
 Ala Phe Ala His Arg Pro Glu His Lys Thr Ser Asp Ser Thr Phe Leu  
           115                  120                  125  
 Val Phe Met Ser His Gly Ile Arg Glu Gly Ile Cys Gly Lys Lys His  
   130                  135                  140  
 Ser Glu Gln Val Pro Asp Ile Leu Gln Leu Asn Ala Ile Phe Asn Met  
 145                  150                  155                  160  
 Leu Asn Thr Lys Asn Cys Pro Ser Leu Lys Asp Lys Pro Lys Val Ile  
                   165                  170                  175  
 Ile Ile Gln Ala Cys Arg Gly Asp Ser Pro Gly Val Val Trp Phe Lys  
           180                  185                  190  
 Asp Ser Val Gly Val Ser Gly Asn Leu Ser Leu Pro Thr Thr Glu Glu  
   195                  200                  205  
 Phe Glu Asp Asp Ala Ile Lys Lys Ala His Ile Glu Lys Asp Phe Ile  
   210                  215                  220  
 Ala Phe Cys Ser Ser Thr Pro Asp Asn Val Ser Trp Arg His Pro Thr  
 225                  230                  235                  240  
 Met Gly Ser Val Phe Ile Gly Arg Leu Ile Glu His Met Gln Glu Tyr  
           245                  250                  255  
 Ala Cys Ser Cys Asp Val Glu Glu Ile Phe Arg Lys Val Arg Phe Ser  
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Thr Leu Thr Arg Cys Phe Tyr Leu Phe Pro Gly His  
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